Reviewer's report

Title: Cost-effectiveness of clostridial collagenase ointment on wound closure in patients with diabetic foot ulcers: economic analysis of results from a multicenter, randomized, open-label trial

Version: 1 Date: 11 May 2014

Reviewer: Shan Bergin

Reviewer's report:

I have been asked to review this paper primarily from a wound care perspective. Given I am not commenting in detail on the modelling used in this paper I will list my comments below as a narrative as opposed to using the specific headings above.

I don't believe this paper will hold wide appeal for the readers of JFAR. The modelling used is extremely technical and as described by the authors is not easily understood by the 'lay person'. I feel there are issues with the methods used to evaluate the wound care product that is the subject of the economic analysis and although I have only a very basic understanding of the Markov model used for forward cost projection I am not convinced that the model took into account the truly multifactorial nature of DFUs. There are several variables that determine whether a DFU re-occurs (biomechanics, off-loading, footwear, compliance) or stays healed and I wasn't convinced that the modelling takes all of these into account. Other comments/queries are listed below:

- "CCO is often used......." I am not aware of this product being available in Australia so I feel this comment is not accurate. How do the authors judge how widely it is used elsewhere?

- The reference to the effectiveness of Santyl on Pressure Ulcers is not transferable to DFU as the aetiology and physiology of the wounds is very different

- As the authors discuss the sample size is small

- both the treatment and follow up periods are short in terms of provision of wound care and it is not clear to me what care if any was provided in the follow up phase

- according to the results the cost of care provided was virtually the same during the actual study period and only swings in favour of CCO during the economic modelling, this will be of little interest to the working clinician who will work in a health care environment that is very focussed on short term outcomes only

- the dressings used on the control group are not necessarily appropriate comparators with CCO as according to the authors CCO is primarily a debriding agent whereas Silver dressings including Silver Sulphadiazine which made up over 50% of the control group are for use in managing infection and exudate. So
in essence the authors are not comparing like with like. Given that Silver based dressings are also very expensive does this perhaps bias the comparison of costs with use of CCO? The use of the Hydrogel in one of the control group participants would have made an interesting comparison as it is used as a form of debridement and also is a lot cheaper than anything silver based so may have come out in favour of the control.

- during the treatment phase of the study the wounds were dressed daily however economic modelling was based on weekly dressings?

- This maybe just my ignorance with relation to the modelling however I am not sure why death is included as part of the analysis?

- Looking at the wound measurements recorded it appears the wounds treated with CCO started to increase in size again post treatment phase however those in the control group stayed the same, so again it doesn't appear the use of CCO is more beneficial until the modelling projection is undertaken.

- Given the authors are discussing "epithelialised weeks" are they suggesting that CCO promotes generation of more robust new epithelium that is less likely to re-ulcerate?

- There is no detail on the types of off-loading used- was this factored in to the cost of treatment?

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.